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Joint articulation increases proteoglycan release from cartilage in the presence of IL-1ß

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Purpose: There is an increase in IL-1ß following joint injury which up-regulates catabolic enzymes breaking down the cartilage matrix. Little is known about the added effect of joint motion on matrix degradation. In this in vitro study we investigated proteoglycan/GAG-release, an indicator for matrix break-down, using a joint simulator applying dynamic loads and articular motion onto living cartilage explants in the presence of IL-1ß.
Methods and Materials: Bovine stifle joints of 24-week-old animals were obtained from a local abattoir within 24 hours of slaughter. Nine cartilage disks were removed from the trochlea using a 14mm punch. After a 5 day pre-culture, 3 disks were tested in a joint simulator in the presence of 10ng/ml IL-1ß (motion+IL-1), 3 were tested in carrier media + IL-1 ß (no motion+IL-1) while the remaining disks served as controls. All tests were performed in serum-free, DMEM:F12 media for 3 hours. Medium was then individually collected and analyzed for the presence of proteoglycans/GAGs using the DMMB assay.
Results: Cartilage explants cultured in the presence of IL-1ß (no motion+IL-1) resulted in a 1.5-fold increase in proteoglycan/GAG release when compared to control. When motion was applied (motion+IL-1), there was a 4-fold increase in proteoglycan/GAG release when compared to control and a 2.6-fold increase when compared to 'no motion+IL-1'.
Conclusions: The combination of joint articulation and IL-1 ß resulted in the highest amount of proteoglycan/GAG release into the media. This preliminary evidence suggests that joint articulation following joint injury may be detrimental to the cartilage matrix.

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Increase in SZP synthesis of cartilage by articular stimulation with migrating contact

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Purpose: The contribution of mechanical stimuli in regulating superficial zone protein (SZP) synthesis in synovial joints and chondrocyte-seeded scaffolds has been reported. This study was aimed towards determining the effect of dynamic compressive loading and articular motion on the SZP synthesis of articular cartilage explants.
Methods and Materials: Full thickness cartilage explants were procured from the trochlea and femur of two freshly harvested 6-8 months old bovine knees. After pre-culturing for 5 days in 10% FBS DMEM F12 media, the explants were loaded for two 1-hour cycles per day for 4 days in a joint simulator. Analogous to the natural knee, the simulator counterface, an alumina ball, articulated on the cartilage explant back and forth. This resulted in a migration of contact area. It has been reported that a migrating contact maintains a low friction coefficient. Between loadings, cartilage explants were allowed to swell freely in medium. Conditioned medium was collected and replaced daily. ELISA assays were performed on the media collected on days 5 and 11 to measure the SZP accumulation. For analysis, the ratio of the end-to-start day was computed. Free swelling explants served as controls.
Results: SZP synthesis increased 2.75-folds in the articular motion group, from day 5 to 11, compared to a 1.56-fold increase in controls. This difference was significant ($p<0.05$, ANOVA).
Conclusions: Supporting our hypothesis, articular motion increased the SZP synthesis of cartilage explants. Based on earlier investigations the possibility of SZP being mechanically sheared off from the cartilage surface appears unlikely but needs to be further investigated.

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Anatomical site and treatment modulate early repair of cartilage focal defects in a caprine model

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Purpose: Determine the effect of anatomical site and treatment on early repair of cartilage focal defects in a caprine model.
Methods and Materials: Two full-thickness osteochondral defects (4.5mm diameter, 10mm depth) were created unilaterally in the medial femoral condyle and the lateral patellar groove of adult goats [Lane, 2004]. In each location, one defect was left empty while the other defect was filled with an autograft plug. The animals were sacrificed at 12 weeks and the defects were scored macroscopically [ICRS Cartilage Injury Evaluation Package] and histologically [Sellers, 2000]. Data were analyzed using two-factor ANOVA.
Results: Gross scores and histological scores for defect filling, integration with the adjacent cartilage, and surface smoothness were significantly higher in the groove than in the femoral condyle, independent of treatment group. Anatomical site did not significantly modulate reformation of the tidemark, replacement of the subchondral bone, or Safranin-O staining intensity. Scores for autografts were significantly higher than those for empty defects. Defects with autografts had better defect filling, Safranin-O staining, cellular morphology, replacement of the subchondral bone, and reformation of the tidemark than those left empty.
Conclusions: This study demonstrates the importance of anatomical site and treatment on the early assessment of cartilage repair after only 12 weeks. These differences may be related to mechanical loading, vascularization of the subchondral bone, or other factors. The effect of anatomical site on cartilage repair has not been extensively documented and needs to be further evaluated to better understand its importance in large animal pre-clinical models.

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Tissue engineerined total meniscus replacement – 12 months results in a sheep model

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Purpose: The aim of the study was to investigate the use of a novel hyaluronic acid/polycaprolactone material for meniscal tissue engineering and to evaluate the tissue regeneration after the augmentation of the implant with expanded autologous chondrocytes.
Methods and Materials: 26 skeletally mature sheep were treated with total medial meniscus replacements while 12 meniscectomies served as empty controls. The animals were divided in two groups: cell free scaffold or scaffold seeded with autologous chondrocytes. Two different surgical techniques were compared: in 12 animals the implant was sutured to the capsule and to the meniscal ligament and in the other 14 animals also a transtibial fixation of the horns was used. The animals were euthanized after 12 months. The specimens were assessed by gross inspection and histology.
Results: All implants showed excellent capsular ingrowth at the periphery. Macroscopically, no difference was observed between Cell Seeded and Cell Free group. Better implant appearance and integrity was observed in the group without trans-osseous horn fixation. Cartilage degeneration was significantly less in the joints with implants than in the meniscectomy joints. The histological investigation revealed tissue formation, cellular infiltration and vascularisation. Cartilaginous differentiation was significantly more commonly seen in the cell seeded constructs.
Conclusions: The current study supports the idea that a novel HA-PCL scaffold has the potential for total meniscal substitution. Seeding of the scaffolds with autologous chondrocytes leads to more mature fibrocartilarginous tissue differentiation. Although cartilage degeneration is not totally prevented the implants provide cartilage protection compared to total meniscectomy.